PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	06 June 2005 (06.06.2005)
Applicant's or agent's file reference PAT2786W-90	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA2005/000323	02 March 2005 (02-03-2005)	02 March 2004 (02-03-2004)

International Patent Classification (IPC) or both national classification and IPC
A61K 31/167 A61P 29/00 A61P 11/00 A61P 31/00

Applicant
MCGILL UNIVERSITY ET AL

1. This opinion contains indications relating to the following items :

[X]	Box No. I	Basis of the opinion
[X]	Box No. II	Priority
[X]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement.
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[X]	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001(819)953-2476	Authorized officer Tania Nish (819) 934-3592

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2005/000323

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] This opinion has been established on the basis of a translation from the original language into the following language ,which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      [ ] a sequence listing

      [ ] table(s) related to the sequence listing

   b. format of material

      [ ] in written format

      [ ] in computer readable form

   c. time of filing/furnishing

      [ ] contained in the international application as filed.

      [ ] filed together with the international application in computer readable form.

      [ ] furnished subsequently to this Authority for the purposes of search.

3 [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statement that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. [X] The following document has not yet been furnished :

   [X] copy of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(a)).

   [ ] translation of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. [ ] This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary :

   The priority document pertaining to the present application has not been checked as it was unavailable at the time of establishing this first written opinion. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is incorrect, the document, WO 2004/064823 A1, cited in the international search report could become relevant in assessing whether claims 1-5 meet the criteria set forth in Article 33(2-4) PCT.

Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of :

[ ] the entire international application

[X] claim Nos. 1-5

because:

[X] the said international application, or the said claim Nos. 1-5
relate to the following subject matter which does not require an international preliminary examination *(specify)* :

Claims 1-5 are methods of medical treatment. (Rule 39.1(iv) PCT)
Although claims 1-3 are directed to methods of medical treatment of the human/animal body, the search has been carried out based on the alleged effects of fenretinide and derivatives/analogs and ceramide and derivatives/analogs on pro-inflammation, inflammatory response and proliferation and respiratory tract infection

The subject matter of claims 1-5 is directed to a method of medical treatment of the human or animal body (Rule 39.1(iv)PCT). No unified criteria exist in the PCT Contracting States for the assessment of the industrial applicability of claims 1-5 (Article 33(4)PCT).

[X] the description, claims or drawings *(indicate particular elements below)* or said claim Nos. 1-5
are so unclear that no meaningful opinion could be formed *(specify)* :

Present claims 1-5 relate to a method to treat inflammation with a compound that increases ceramide levels in the cell. The claims cover an extremely large number of possible compounds, including currently undiscovered compounds. As such, the extremely large number of options of compounds renders the claims unclear and not concise within the meaning of Article 6 PCT that a meaningful search is not possible. Consequently, the search has been carried out for only a limited number of compounds which are disclosed in the disclosure, namely fenretinide and derivatives/analogs thereof and ceramide and derivatives/analogs thereof.

[ ] the claims, or said claims Nos. are so inadequately supported
by the description that no meaningful opinion could be formed.

[ ] no international search report has been established for said claims Nos.

[ ] the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that :

the written form [ ] has not been furnished

[ ] does not comply with the standard

the computer readable form [ ] has not been furnished

[ ] does not comply with the standard

[ ] the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

[ ] See Supplemental Box for further details.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2005/000323

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims		YES
	Claims	1-5	NO
Inventive step (IS)	Claims		YES
	Claims	1-5	NO
Industrial applicability (IA)	Claims		YES
	Claims		NO

2. Citations and explanations :

D1: CA 2 365 290 A1
D2: WO 01/72701 A1
D3: Am. J. Respir. Cell Mol. Biol., 22, 460-468
D4: WO 00/00207 A1
D5: J. Biol. Chem., 277, 49531-49537
D6: JNCI, 91, 1138-1146
D7: WO 2004/0644823 A1

NOVELTY

1) D1 discloses the use of ceramides, derivatives and/or precursors of ceramides in the treatment of cystic fibrosis and associated diseases and illnesses, such as inflammation and respiratory infection.

D2 discloses the use of ceramide and derivatives thereof in the prevention of cellular proliferation, inflammatory disease or inflammation.

Therefore, since the subject matter of claims 1-2 and 4-5 is the same as the subject matter disclosed by D1 and D2, claims 1-2 and 4-5 would not be considered novel with respect to D1 and D2. (Art.33(2), PCT)

2) D3 discloses the use of ceramides and analogs thereof in the mediation of cell death by apoptosis. Ceramide is disclosed as a second messanger in initiating the apoptotic response.

D4-D6 disclose the use of fenretinide and other such retinoic acid derivatives in the treatment of hyperproliferative disorders by manipulation of the ceramide-mediated apoptosis.

Therefore, since the subject matter of claim 3 is the same as the subject matter disclosed by D3-D6, claim 3 would not be considered novel with respect to D3-D6 (Art.33(2), PCT)

INVENTIVE STEP

One skilled in ther art with regards to D1-D6 would be able to conclude that the increase of ceramide levels will inhibit inflammation and proliferation and thus use of a medicament that increases ceramide levels, such as fenretinide and other like retinoic acid derivatives and precursors/derivatives of ceramide, will treat inflammation and proliferation. (Art. 33(3), PCT)

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

Claims 1-5 do lack clarity and conciseness and do not comply with Article 6 (PCT) for the following reasons:

1) Claims 1-5 defines the compound used in the treatment as "an agent that increases ceramide levels in the cell". The definition attempts to define the therapeutic compound of the invention solely by the result to be achieved, i.e. the increase of ceramide levels in the cell. Therefore rendering the claims unclear, as it directs to a desired results rather than to the combination necessary to achieve the result as described in the description.

2) Claims 1-2 and 4-5 define the use of an agent to treat inflammatory response, proliferation and reduction of respiratory tract infections. The description specifically supports the treatment of respiratory inflammation, proliferation and respiratory infection in subjects with cystic fibrosis (CF) disease using a specific agent, namely fenretinide. Therefore, the claims are broader than the scope of the invention disclosed in the description.

3) The term "diseased cell" in claims 1 and 4 cause the claims to be ambiguous

4) Claim 3 defines the use of an agent to induce an inflammatory response in a cell. The claim is broader than the scope of the invention as taught in the description where fenretidine is shown to induce an inflammatory response in cells that are not in a pro-inflammatory response, ie cell which are not stimulated.